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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/599,226	02/09/96	SALFELD	J BBI-043

18M1/0805

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EXAMINER
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EISENSCHENK, F

ART UNIT	PAPER NUMBER
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1816

DATE MAILED: 08/05/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5/6/97

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-64 is/are pending in the application.

Of the above, claim(s) 24-43, 47-64 is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1-23, 44-46 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

1. The election of claims 1-23 and 44-46, without traverse, in paper #7 is noted. Applicant is requested to cancel all on-elected claims. Claims 24-43 and 47-64 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.
2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.
3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The specification is objected to and claims 1 and 3 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) can be reproducibly isolated; or (3) deposited.

It unclear if a cell line which produces an antibody having the exact structural and chemical identity of D2E7 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed, especially since it is not possible to compare antibodies made outside the teachings of this application with antibodies having the characteristics disclosed herein. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

5. Claims 1-23 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification fails to provide any teachings as to how one skilled in the art is to obtain human antibodies having the recited characteristics. As an example, there is no teaching as to the origin of the D2E7 antibody or how this antibody was obtained. Absent such teaching, one skilled in the art has no means by which to obtain antibodies within the scope of the claims since the manner with which such antibodies are to be isolated is

not taught. There is no teaching as to where and/or how one skilled in the art is to make antibodies having the recited characteristics. The specification teaches that naturally occurring human antibodies, generally, have low binding affinities for human TNF- $\alpha$ , see specification, page 2, lines 7-34. Thus, one skilled in the art would be subjected to undue experimentation in order to practice the invention as currently claimed.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
  - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).
8. Claims 1-23 and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (EMBO J.) In view of Lewis et al. (WO 95/23813) or Lewis et al. (J. Cell. Biochem.). Claims 1-23 and 44-46 are drawn to human TNF- $\alpha$  antibodies. Griffiths teach human antibodies to TNF- $\alpha$  derived from phage display libraries. The reference differs from the claimed invention in that the binding affinities and kinetics of antigen binding differ from those of the claimed human monoclonal antibodies. Both Lewis references teach the use of alanine scanning mutagenesis to increase the binding affinities and improve the kinetics of antigen binding of monoclonal antibodies. Observed improvements in antigen binding as high as eleven fold have been observed by Lewis et al. (See page 3, PCT '492, about line 25). Lewis et al. also noted ten-fold slower antigen dissociation rates with antibodies produced using alanine scanning mutagenesis (see PCT '492, page 4, lines 14-22).

One of ordinary skill in the art at the time the invention was made would have been motivated to utilize alanine scanning mutagenesis to produce and select human TNF- $\alpha$

specific monoclonal antibodies having high binding affinities, slow dissociation constants, and improved antigen kinetics because such antibodies would have been useful for the production of diagnostic and therapeutic antibodies. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. No claim is allowed.
10. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 308-4242.
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Eisenschenk whose telephone number is (703) 308-0452. The examiner can normally be reached Monday through Thursday from 6:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.



August 4, 1997

Christopher Eisenschenk, Ph.D.

Primary Examiner

Group 1800